Travel patterns, risk behaviour and health problems of travellers with rheumatic diseases compared to controls: A multi-centre, observational study

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Abstract: BACKGROUND Patients with chronic conditions travel around the world more than ever. Only few studies have examined travel patterns and health outcomes of patients with rheumatic diseases during international travel. METHOD We conducted a multi-centre prospective cohort study in Switzerland, in which we studied the immunogenicity and safety of vaccinations in patients with rheumatic diseases and travellers without rheumatic diseases (controls). Participants who travelled internationally received questionnaires 1 and 13 weeks post-travel. We compared travel patterns, risk behaviours, and travel-associated problems during and after the trips in both groups. RESULTS 274 participants returned post-travel questionnaires (65 rheumatic patients, 209 controls). Controls more frequently travelled to subtropical/tropical destinations and stayed longer abroad. 64% of all participants experienced health problems during travel (74% rheumatic patients vs. 62% controls, P = 0.11). Pre-travel, patients reported a higher susceptibility to gastrointestinal infections. During travel, a higher percentage of rheumatic patients cancelled the day programme due to health problems (13% vs. 4%, P = 0.024). The main problems in rheumatic patients occurred due to the underlying rheumatic diseases, or were of psychological nature. Although not statistically significant, infectious disease symptoms (rhinitis, cough) occurred more frequently in controls. When only considering subtropical/tropical destinations, rheumatic patients more frequently had gastrointestinal problems during travel - and skin infections after the trip. CONCLUSIONS This study does not support the notion that patients with rheumatic diseases should avoid international travel for an increased risk of infections. In patients with subtropical/tropical destinations, however, gastrointestinal problems may be increased during travel - and skin infections post-travel.

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Travel patterns, risk behaviour and health problems of travellers with rheumatic diseases compared to controls: a multi-centre, observational study

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Key words

rheumatic disease, immunosuppression, travel, health problems, risk behaviour

Abstract

Background: Patients with chronic conditions travel around the world more than ever. Only few studies have examined travel patterns and health outcomes of patients with rheumatic diseases during international travel.

Method: We conducted a multi-centre prospective cohort study in Switzerland, in which we studied the immunogenicity and safety of vaccinations in patients with rheumatic diseases and travellers without rheumatic diseases (controls). Participants who travelled internationally received questionnaires 1 and 13 weeks post-travel. We compared travel patterns, risk behaviours, and travel-associated problems during and after the trips in both groups.

Results: 274 participants returned post-travel questionnaires (65 rheumatic patients, 209 controls). Controls more frequently travelled to subtropical/tropical destinations and stayed longer abroad. 64% of all participants experienced health problems during travel (74% rheumatic patients *vs.* 62% controls, P=0.11). Pre-travel, patients reported a higher susceptibility to gastrointestinal infections.

During travel, a higher percentage of rheumatic patients cancelled the day programme due to health problems (13% *vs.* 4%, P=0.024). The main problems in rheumatic patients occurred due to the underlying rheumatic diseases, or were of psychological nature. Although not statistically significant, infectious disease symptoms (rhinitis, cough) occurred more frequently in controls. When only considering subtropical/tropical destinations, rheumatic patients more frequently had gastrointestinal problems during travel - and skin infections after the trip.

Conclusions: This study does not support the notion that patients with rheumatic diseases should avoid international travel for an increased risk of infections. In patients with subtropical/tropical destinations, however, gastrointestinal problems may be increased during travel - and skin infections post-travel.

1. Introduction

International tourism grew by 4% between January-September 2019 according to the World Tourism Organization (UNWTO) compared to the same period in the previous year and further increases might be expected[1]. As new medical care and treatment options have been developed over the past decades for patients suffering from rheumatic disorders, these patients feel healthier and often lead a life-style comparable to that of healthy persons. As a consequence, international travel has also increased in this patient group[2,3].

Only few investigators have assessed health risks related to travel in tropical countries in rheumatic disease patients. Wieten et al. examined the health risks of a heterogeneous group of immunocompromised travellers. The data suggest that travellers with underlying conditions were at an increased risk for travel related diseases, especially for gastrointestinal symptoms[4]. Baaten et al. examined whether or not travellers on immunosuppressants with various underlying diseases had a higher incidence of health problems during international travel than healthy travellers. The authors found skin infections more often in immunosuppressed travellers than in controls[5]. No other symptomatic infections appeared more frequently in immunosuppressed compared to non-immunocompromised travellers.

In recent years, persons with rheumatic diseases have constituted a large proportion of immunocompromised travellers[6]. They have an increased risk of infection, partly because of the underlying conditions per se, and partly due to taken immunosuppressive medications[7–10]. The risk for influenza infection[11,12], pneumococcal pneumonia[13], primary varicella infection[14] and herpes zoster[15] is elevated in rheumatic patients compared to the general population.

An increased risk for specific diseases from subtropical or tropical countries, such as malaria, dengue and hepatitis A has not been described in the literature. Travel associated infections may have a more severe course in immunocompromised individuals, as demonstrated for tuberculosis on tumour necrosis factor alpha inhibitor therapy[2,16].

Although the vulnerability and exposure to health risks of travellers depends on the destination, duration and behavioural factors[17–19], little is known about rheumatic disease patients´ travel destinations and behaviour, their incident health problems and evolution of disease activity.

In the context of a prospective vaccination study in patients with rheumatic diseases and travellers without rheumatic diseases (controls) we sent post-travel questionnaires to those with an international trip with the aim of comparing travel patterns, risk behaviours, travel-associated problems and needs in patients with rheumatic diseases and controls. Furthermore, we studied the effects of travel on rheumatic disease activity.

2.1. Study design

This study investigating travel issues was nested within a multi-centre prospective cohort study (ClinicalTrials.gov Identifier: NCT01947465) in 6 rheumatology and 2 travel clinics in Switzerland. In that particular study the immunogenicity and safety of a hepatitis A and/or tetanus/diphtheria booster vaccination was prospectively studied (details on study design and recruitment described in [20]). Control participants (individuals without rheumatic diseases) were recruited in the travel clinics, patients with rheumatic diseases were recruited in travel clinics and rheumatology clinics, with a preponderance being enrolled in the rheumatology clinics.

Participants were recruited between January 2014 and December 2015. We sent out the travel questionnaires to participants of the vaccination study who travelled internationally (1week and 13 weeks after their return). A prepaid return envelope was included. The 1-week post-travel questionnaire contained questions on the following domains: a) travel patterns (destinations, length of stay, travel style, place of stay, activities during the trip), b) risk behaviours (food hygiene, protection from mosquito bites, contact with animals), c) travel associated health problems (e.g. fever, gastrointestinal problems, respiratory infections, skin infections, urinary tract infections, accidents), d) rheumatic disease activity: worsening or improvement of disease symptoms (e.g. arthralgia, joint swelling), e) travel-associated incidents (requirement of medical assistance, change of original travel plans due to health issues). The 1-week questionnaire comprised questions on risk behaviours and health problems during the trip and health problems that occurred up to 1 week after the return. It also included a section on the participants' own perception regarding their vulnerability to infections and other health problems before the trip. They were asked to rate their vulnerability on a scale from 1 (hardly susceptible) to 5 (very susceptible).

In the 13-week post-travel questionnaire we assessed whether or not the health problems and medical needs differed between patients with rheumatic diseases and controls during the 13 weeks after their return from the trip.

2.2. Study population

Rheumatic patients were recruited consecutively into the study if they had one of the following underlying conditions: rheumatoid arthritis (RA), axial spondyloarthritis (SpA), peripheral psoriatic arthritis (PsA), or vasculitis (Behçet's disease or ANCA-associated vasculitis). All participants were aged 18 years and above. If patients took one of the following medications in the respective time period they were classified as immunosuppressed: systemic corticosteroids, methotrexate, or etanercept within the past month; azathioprine within the past two months; other conventional synthetic disease modifying anti-rheumatic drugs (csDMARDs), adalimumab, certolizumab, golimumab, infliximab, and other biological DMARDs within the past three months; leflunomide within the past six months; and rituximab in the past 12 months [21,22].

The study was approved by the Aargau-Solothurn, Bern, Geneva, Nordwestschweiz, St. Gallen and Zurich Ethics committees (Reference numbers EK Aargau-Solothurn: 2013/062, Bern: 182/13, CCER 2016-00218, EKNZ 257/13, EKSG 13/138, KEK-ZH 2013-0188). All participants signed an informed consent prior to study enrolment.

2.3. Statistics

The analysis was executed with Stata 14.0 (Stata Corp. LP, Texas, USA). For evaluation of differences in proportions we used a chi-squared or Fisher's exact test, as appropriate. The Wilcoxon rank-sum test was used to compare independent samples with continuous data that had a non-normal distribution.

3.1. Travellers' demographics

Participants travelled between January 2014 and May 2016. Overall, 654 participants were enrolled in the vaccination study (349 with rheumatic diseases and 305 controls). 274 (42%) participants returned a completed post-travel questionnaire; 189 completed both the 1-week and the 13-weeks post-travel questionnaires, 58 persons only the first questionnaire and 27 only the second. 65 (19%) travellers with rheumatic diseases returned a questionnaire and 209 (67%) travellers without rheumatic diseases sent the completed questionnaire back. Sex and age did not differ between the group who returned a post-travel questionnaire and the one who did not. The baseline disease activity score did not differ in patients with rheumatoid arthritis or peripheral psoriasis who returned a post-travel questionnaire and those who did not. Participants with spondyloarthritis who returned the post-travel questionnaires had lower disease activity scores on a median than those who did not return the questionnaires (Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) 2.45 *vs.* 4.40).

Travellers with rheumatic conditions had rheumatoid arthritis (n=28, 43%), spondyloarthritis (n=19, 30%), vasculitis (n=8, 12%), and peripheral psoriatic arthritis (n=10, 15%). The majority of participants (n=56, 86%) received immunosuppressive drugs at the time of travel. 14 were on corticosteroid treatment, 24 had conventional DMARDs (cDMARDs). 23 were treated with tumour necrosis factor alpha inhibitors, and 14 received other biological disease modifying anti-rheumatic drugs (bDMARD).

Travellers with rheumatic diseases were more often female than travellers without rheumatic diseases (68% *vs.* 54%, P=0.052). The median age was comparable between participants with and without

rheumatic conditions (48.5 years, IQR 34.6-57.3 *vs.* 48.9, IQR 31.7-61.0, P=0.89, Table 1). Patients also more often had other chronic medical conditions than the controls (51% *vs.* 27%, P<0.001).

3.2. Travel reasons and destinations

While 96% of journeys led to subtropical/tropical areas in controls, only 59% of destinations in travellers with rheumatic diseases were subtropical/tropical. Among patients on immunosuppressive therapies, 22 (45%) undertook a trip to a subtropical/tropical country. The remaining trips led to Europe or North America (Table 1). More than 80% of trips were undertaken for touristic reasons in both groups. Controls stayed longer abroad than rheumatic patients (18 days, IQR 14-24 *vs.* 14 days, IQR 8-24, P=0.0074, Table 1).

3.3. Travel style

Controls often travelled more luxuriously than rheumatic patients (30% *vs*. 23%, P=0.37, Table 1). Rheumatic patients noted "by foot" as their main mode of transport more often than controls (28% *vs.* 7%, P<0.001). The results did not change when we compared immunosuppressed and non-immunosuppressed travellers (non-immunosuppressed containing not-immunosuppressed patients and controls).

More than 50% of all travellers stayed at a beach during their travels and a similar percentage visited cities and cultural sites. Slightly more controls than rheumatic patients undertook trekking activities (18% *vs.* 14%, P=0.46). Compared to rheumatic patients, trekking in controls often included great physical efforts (48% *vs.* 38%, P=0.58), altitude differences of more than 1,000m (52% *vs.* 29%, P=0.27) and longer durations (53% *vs.* 38%, P=0.43). Around 5% in both groups stayed in areas where time to medical access would have taken more than 24 hours (Table 1).

Nearly 35% of all subjects reported a contact with warm-blooded animals (Table 1). While no rheumatic patients were bitten or scratched nor had open wounds licked by mammals, 6 control subjects reported such an incident. Apart from controls drinking more beer, no difference in drinking behaviour/hygiene concerning beverages was noted, also when only travellers with subtropical/tropical destinations were looked at (Table 2).

Regarding food hygiene, patients with rheumatic diseases demonstrated a more cautious behaviour than the control group. They ate less often at food stands (16% *vs.* 28%, P=0.064), ate raw fish less often (10% *vs.* 21%, P=0.076), ate fruit that they had not peeled themselves less frequently (35% *vs.* 57%, P=0.003), and less salads prepared by others (57% *vs.* 70%, P=0.067).

When comparing eating behaviour only in those participants travelling to subtropical/tropical countries, more patients ate raw meat and self-prepared salads (Table 2).

More controls than patients used mosquito protection during the day, evening and night. The difference became less distinct when comparing only those travelling to subtropical/tropical destinations (day, 86% *vs.* 76%, P=0.13; night, 77% *vs.* 70%, P=0.41, Table 2).

Controls and patients obtained travel health insurance and insurance including repatriation for the trip with equal frequency (around 50%, Table 1).

A travel pharmacy, including antibiotics and alkaline soap, was carried by one fifth of patients and controls (17% and 19%). Controls were more likely to carry sunscreen with them (94% *vs.* 74%, P<0.001). The difference stayed noteworthy when comparing only those travelling to subtropical/tropical destinations (92% *vs.* 77%, P=0.044).

3.5. Health problems before the trip

Regarding the vulnerability to airway infections, urinary tract infections, skin lesions and skin infections in Switzerland, no differences between rheumatic disease patients and controls were reported. However, patients reported a higher susceptibility to gastrointestinal infections prior to travel (P=0.01 data not shown, questionnaire on health problems in supplementary).

3.6. Health problems during the trip

Overall, 64% of travellers reported health problems during their trip. Slightly more rheumatic disease patients than controls had health issues during the trip (74% *vs.* 62%, P=0.11, Figure 1 (A)).

When only looking at health problems in travellers to subtropical/tropical destinations, 87% of rheumatic patients and 62% of controls experienced health problems (P=0.006, Figure 1 (B)). Nightmares were experienced by 19% of patients and 8% of controls (P=0.047). Rheumatic disease patients felt fatigued considerably more often (43% *vs.* 16%), tense (21% *vs.* 4%) and depressed (28% *vs.* 4%) than controls (all P<0.001). Patients and controls reported gastrointestinal problems with the same frequency (31% *and* 30%, P=0.87) when looking at all destinations. In the participants travelling only to subtropical/tropical destinations, 52% of rheumatic patients and 32% of controls had gastrointestinal problems (P=0.03, Figure 2 (B)). Skin infections were reported to a similar extent in both groups (overall: rheumatic 9%, controls 8%, P=0.74; subtropical/tropical: rheumatic 11%, controls 8%, P=0.61).

Overall, more controls had cough (18% *vs.* 12%, P=0.35). More patients than controls used antibiotics (10% *vs.* 6%, P=0.15) and medications against fever/pain (49% *vs.* 29%, P<0.001) during the trip. Only controls used anti-malarials for self-treatment (3%); none of the patients did.

Nearly 9% of all participants experienced an accident during the trip (n=22, controls: 17, patients: 5). Of these, 43% had an accident as a pedestrian (n=9); controls more often than patients (50% (n=8/17) *vs.* 20% (n=1/5)); 14% had a sports injury (6% (n=1/17) *vs.* 40% (n=2/5)), 10% had a motorbike

accident (6% (n=1/17) *vs.* 20% (n=1/5)) and 33% had an accident during a different activity (38% (n=6/17) *vs.* 20% (n=1/5)) (data not shown). The findings did not change when comparing immunosuppressed patients to all other travellers. During the trip quantitatively more immunosuppressed patients reported a health problem (75 % *vs*. 62%, P=0.11). We did not detect more infectious diseases in the immunosuppressed when we compared this group with all other travellers.

3.7. Travel plan changes due to health problems

More rheumatic patients had to cancel the planned day programme (e.g. visit to a museum, city tour) due to health problems than controls (13% *vs.* 4%, P=0.024). In 50%, the underlying rheumatic disease caused the disruption. Rheumatic patients more often had to restrict the time spent with planned activities due to health problems (25% *vs.* 5%, P<0.001) and it was more strenuous for rheumatic patients to follow the planned daily activities (21% *vs.* 3%, P<0.001, Table 1).

3.8. Health problems in the first week after the trip

In the first week after the trip rheumatic disease patients reported drastically more health problems than controls (54% *vs.* 33% P=0.006, Figure 1 (A)). A similar picture was seen when only those participants travelling to subtropical/tropical destinations were looked at (63% *vs.* 33%, P=0.002, Figure 1 (B)). Overall, patients experienced more sleep problems than controls (29% *vs.* 15%, P=0.095), they also felt more often fatigued (52% *vs.* 29%, P= 0.033), tense (25% *vs.* 7%, P=0.013) and depressed (22% *vs.* 8%, P=0.062).

The frequency of gastrointestinal problems, fever and cough decreased in the first week after travel in both groups. Patients still slightly more frequently reported gastrointestinal symptoms (all destinations: 11% *vs.* 10%, P=0.87, subtropical/tropical destinations: 18% *vs.* 11%, P=0.26); controls

more often reported cough (16% *vs.* 13%, P=0.64) and the occurrence of fever was similarly distributed between both groups, irrespective if all or only subtropical/tropical countries were looked at (Figure 1 (A) and (B)). One week after the trip, skin infections were reported more frequently in the rheumatic patient group than in controls (overall: rheumatic 6%, controls 0%, P=0.047; subtropical/tropical: rheumatic 5%, controls 0%, P=0.084).

When comparing the number of health events only in the patients on immunosuppression to all other travellers one week after the trip the findings did not change considerably (53% *vs.* 34%, P=0.015). Overall, we did not find more infectious diseases when comparing the immunosuppressed group with all other travellers.

3.9. Health problems in the 13 weeks after the trip

During the 13 weeks after the trip, again rheumatic patients reported more health problems than controls (59% *vs.* 37%, P=0.004, Figure 1 (A)). When comparing the frequency of overall health problems in patients and controls travelling to subtropical/tropical destinations in the 13 weeks after the trip, the difference becomes less distinct (48% *vs.* 38%, P=0.36). More rheumatic disease patients had gastrointestinal problems (all destinations: 17% vs. 6%, P=0.005, subtropical/tropical destinations 18% *vs.* 6%, P=0.015). Overall, 2% of the controls reported skin infections compared to 15% of rheumatic patients (P=0.013; subtropical/tropical countries: 2% *vs.* 13%, P=0.060). Overall, rheumatic patients had more sleep problems than controls (30% *vs.* 12%, P=0.032). Fatigue (58% *vs.* 28%, P=0.005), tension (34% *vs.* 23%, P=0.24) and depression (25% *vs.* 14%, P=0.21) were also still more frequently reported by rheumatic patients than controls.

Overall, controls reported more often coughs (31% *vs.* 21%, P=0.27), rhinitis (26% *vs.* 18%, P=0.41), a sore throat (20% *vs*. 12%, P=0.34), and fever (12% *vs.* 9%, P=0.69).

Again, when comparing health problems 13 weeks after the trip only in the immunosuppressed to the other travellers, the results did not change notably: also more immunosuppressed patients reported a

health problem during this period (56% *vs.* 36%, P=0.02). We did not identify more infectious diseases in the immunosuppressed when comparing the immunosuppressed group with all other travellers.

3.10. Physician consultations and hospitalisations

During the trip, 4% of patients consulted a physician. This percentage increased to 16% in the first week and to 54% in the 13 weeks after the trip. Controls showed an increase of consultations from 3% during the trip, to 6% in the first week after the trip, and to 23% in the 13 weeks after the trip.

During the trip, no participant had to be hospitalised. In the first week after the trip, two rheumatic patients and one control reported a hospital admission. Reasons in rheumatic patients were a bladder tumour and fever; the reason in the control was a hallux-valgus operation.

In the 13 weeks after their travels six rheumatic disease patients and three controls were admitted to hospital. Reasons in rheumatic patients were bacterial infections, a cataract operation, a hallux valgus operation, poisoning, monthly infliximab infusion and a bladder tumour. The reasons in controls were a hallux valgus operation, a transitory ischaemic attack and a myocardial infarction.

3.11. Complaints specific to rheumatic disease patients

Median body pain before the trip in patients with rheumatic diseases was 1 (scale from 0-10, 0 being no pain, 10 worst imaginable pain, IQR 0-4) and during the trip it was reported to be 2 (IQR 0-4, P=0.44). In the 13 weeks after the trip median body pain was 2 (IQR 0-5, P=0.62).

When asked about general musculoskeletal complaints, joint swelling and joint mobility, patients reported a slight worsening during the trip (Figure 2). In the first week after the trip a slight improvement of joint pain and joint mobility was noted compared to before the trip. 13 weeks after

the trip, all rheumatic symptoms (musculoskeletal symptoms, joint pain, joint swelling and joint mobility) were comparable to the status before the trip.

Overall, psychological problems and not infections were the most frequently reported health problem in travellers with rheumatic diseases. Two thirds of all participants reported health problems during their travel. Infections were not a major issue for travellers with rheumatic diseases – although patients with rheumatic diseases are known to suffer generally more frequently from infections [7–15] and despite travel vaccinations may be less immunogenic in this often immunosuppressed group [23,24]. During (74 % *vs*. 62%) and after the trip more patients than controls reported a health problem (54% *vs.* 33% 1 week after the trip; 53% *vs.* 37% 13 weeks after the trip). The main problems in patients were of psychological nature or due to the underlying rheumatic disease. While fatigue was the main symptom in rheumatic disease patients during and after the trip (followed by gastrointestinal problems and by feeling depressed), the most frequent health problems in controls were gastrointestinal problems (during the trip), fatigue, rhinitis (first week after the trip), and cough (13 weeks after the trip).

When we only looked at subtropical/tropical destinations, patients with rheumatic diseases reported more frequently gastrointestinal symptoms during and after travel; skin infections were noted more often after the trip. A higher frequency of gastrointestinal problems and skin infections in travellers with rheumatic diseases to subtropical/tropical destinations than in controls makes our results comparable to the study results by Wieten et al. and Baaten et al. [4,5]. However, the patients in our study also reported a higher susceptibility to gastrointestinal infections than controls before travel. Thus it remains unclear to what extent the gastrointestinal problems were associated with the trip.

A study from Farnham et al. showed that the most common symptoms during travel by tourists to Thailand were mental health problems (exhaustion 80%, mental distress 50%)[25]. Neuropsychiatric problems in travellers have already been reported in other studies. 11.3% of young Israeli (20-25y, healthy) travellers to the tropics reported psychological symptoms[26].

In our study, it is striking how psychological symptoms increased after the trip in rheumatic disease participants and still had a high prevalence 13 weeks after the trip (during a time period, which most probably depicts “normal life”). Although we cannot compare them to data before the trip (only to data after the trip), which is a clear limitation of this study, patients appeared to be psychologically far better off whilst travelling. Interestingly, fatigue and tension also increased in the controls after travelling. It could mean that being away had a positive influence on these health aspects in both, patients and controls. The study by Farnham et al, did not gather pre-and post travel data on psychological well-being. Thus, it is unknown whether mental problems were worse before or after travel. Furthermore, generally young and healthy travellers were included in the study. These two aspects limit a direct comparability with our study.

Every 10th traveller experienced an accident during the trip

Injury is one of the main causes of morbidity and mortality among travellers[27–29]. More than 1.35 million people die each year as victims of traffic accidents and accidents are the leading cause of death for young adults and children aged 5 – 29 years[30]. Farnham et al. reported that 23% travellers in Thailand experienced an accident[25]; in our study, 10% of the participants reported an accident, which is still a considerable number. The difference could be explained by a large variety of travel destinations in our study. It has previously been shown that the risk of an accident for Swiss travellers is highest in Thailand[31]. In addition, our travellers were considerably older than in the Farnham study.

Rheumatic symptoms worsened during the trip

Although we did not examine the relation between musculoskeletal symptoms and specific destinations we found a worsening during the trip for rheumatic problems in general and in particular for arthritic swelling and stiffness. Symptoms could have been affected by weather conditions[32–34]. Studies from Hollander *et al.* and Patberg *et al.* reported that a weather change like rising humidity and falling barometric pressure produced a significant increase of arthritic pain, swelling and stiffness, but results are still inconclusive[34,35]. It has been shown that pre-existing diseases can cause the

main problems in elderly travellers while abroad [36]. Also, in our study we showed that the rheumatic disease itself often detained patients from their planned activities.

Depending on the subject - sometimes patients and sometimes controls showed a riskier behaviour

Risk behaviour in rheumatic patients did not show a clear pattern, e.g. in some aspects food hygiene was more careful in patients and in other regards controls showed a more prudent behaviour. Patients behaved more carefully regarding mammal contact. However, controls used better mosquito protection and carried sunscreen in their travel pharmacy. Considering that skin cancer is one of the most frequent malignancies in immunosuppressed patients[37–39], the latter is a worrying finding.

Strengths and limitations of our study

Travel destinations and travel duration differed between rheumatic patients and controls and thus some results may be inconclusive. One reason for differing travel destinations is that the controls were enrolled in the travel clinics and the majority of patients in the rheumatology clinics. However, we did not find major differences, when we compared risk behaviours only in travellers to subtropical/tropical destinations.

Our study was conducted retrospectively: as participants answered the questionnaires after their trips the data may be confined by recall limitations in both groups.

In our study we depict a real-world scenario of patients with rheumatic diseases and travellers without rheumatic diseases. We studied for the first time non-infectious disease risks in travellers with rheumatic diseases and not only explored health outcomes, but also risk behaviour. However, participant numbers for rheumatic patients were low, and thus our results may not be generalisable.

We performed a sub-analysis in those only travelling to subtropical/tropical destinations; here the participant numbers of patients with rheumatic diseases is even lower; due to the small number of participants with rheumatic diseases we only conducted descriptive analyses. To characterise rheumatic disease patients´ travel behaviour and health outcomes further larger studies are needed.

5. Conclusions

Overall, no hospitalisation in rheumatic disease patients or controls occurred during the trip and no severe diseases were reported by any of the study participants. Although patients on immunosuppressants may be at a generally increased risk of infection, this study (knowing its limitations) does not support the perception amongst many treating physicians and patients that individuals with rheumatic diseases should avoid international travel for an increased risk of infections. However, patients may be at higher risk of gastrointestinal problems when travelling to subtropical/tropical countries and may report of more skin infections after travelling to these destinations. Apart from that, health problems in travellers with rheumatic diseases were particularly of psychological nature during and after travel or caused by underlying rheumatic diseases. Travelling can modify rheumatic symptoms and signs depending on weather conditions. In some aspects rheumatic patients showed a more careful behaviour while travelling, in some aspects a less careful attitude than controls.

Authors' contributions

All authors were involved either in study design, data collection, statistical analysis or data interpretation, and either drafting or revising the manuscript. All authors gave final approval of the manuscript before submission.

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Conflicts of interest

NS, AC, CG, PH, JF, RM, PV, UAW, CH and SB declare no conflicts of interest.

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Figure 1 (A): Health problems in rheumatic disease patients and controls during the trip, 1 week after the trip and 13 weeks after the trip – all destinations (in percentage)

Figure 1 (B): Health problems in rheumatic disease patients and controls during the trip, 1 week after the trip and 13 weeks after the trip - subtropical/tropical destinations (in percentage)

Figure 2: Improvement or worsening of rheumatic symptoms during, 1 week and 13 weeks after the trip compared to before the trip (median). Positive numbers indicate an improvement, 0 means no change and negative numbers indicate a worsening.

Figure 1 (A): Health problems in rheumatic disease patients and controls during the trip, 1 week after the trip and 13 weeks after the trip – all destinations (in percentage)

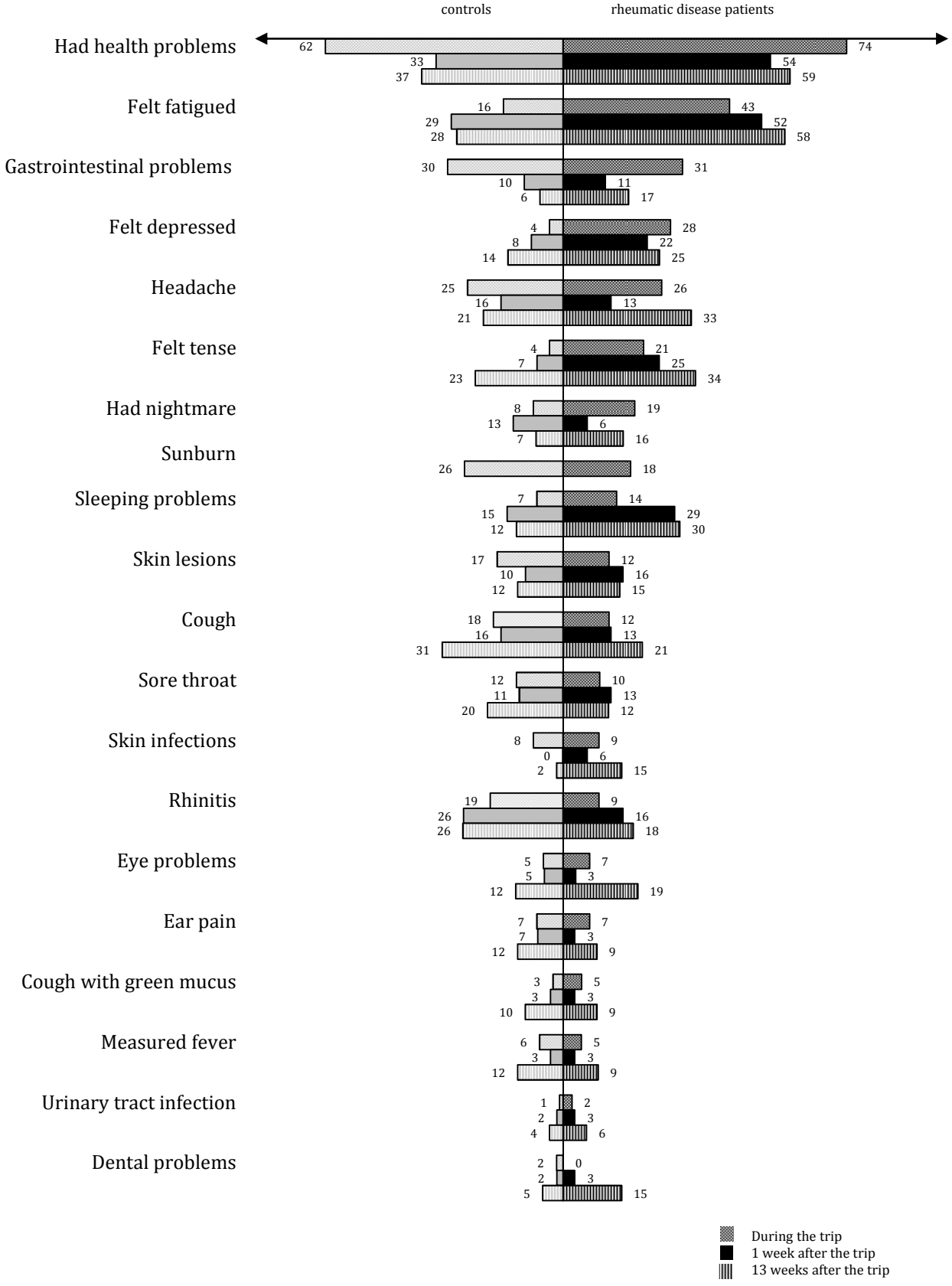

Figure 1 (B): Health problems in rheumatic disease patients and controls during the trip, 1 week after the trip and 13 weeks after the trip - subtropical/tropical destinations (in percentage)

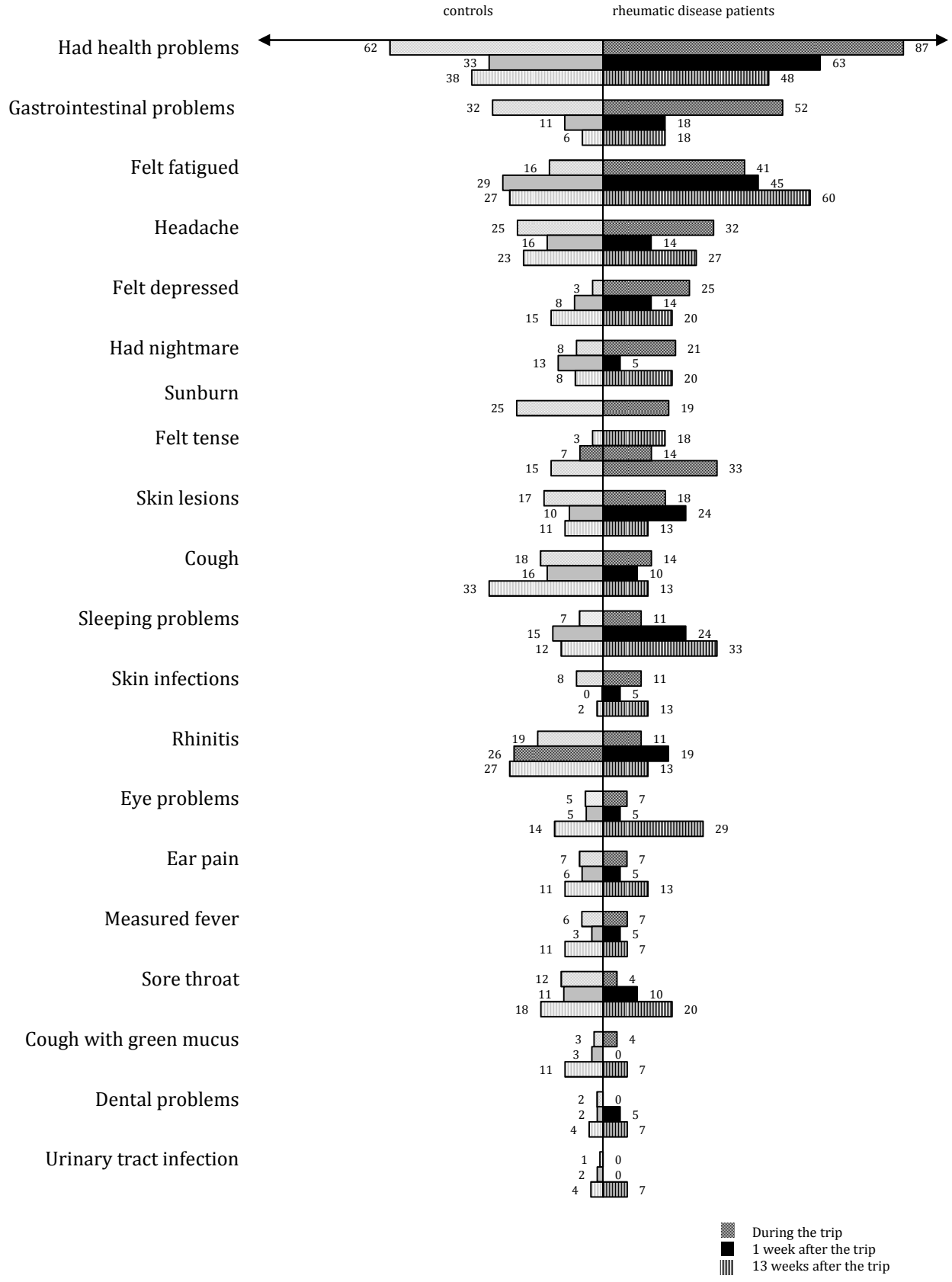

Figure 2: Improvement or worsening of rheumatic symptoms during, 1 week and 13 weeks after the trip compared to before the trip (median). Positive numbers indicate an improvement, 0 means no change and negative numbers indicate a worsening.

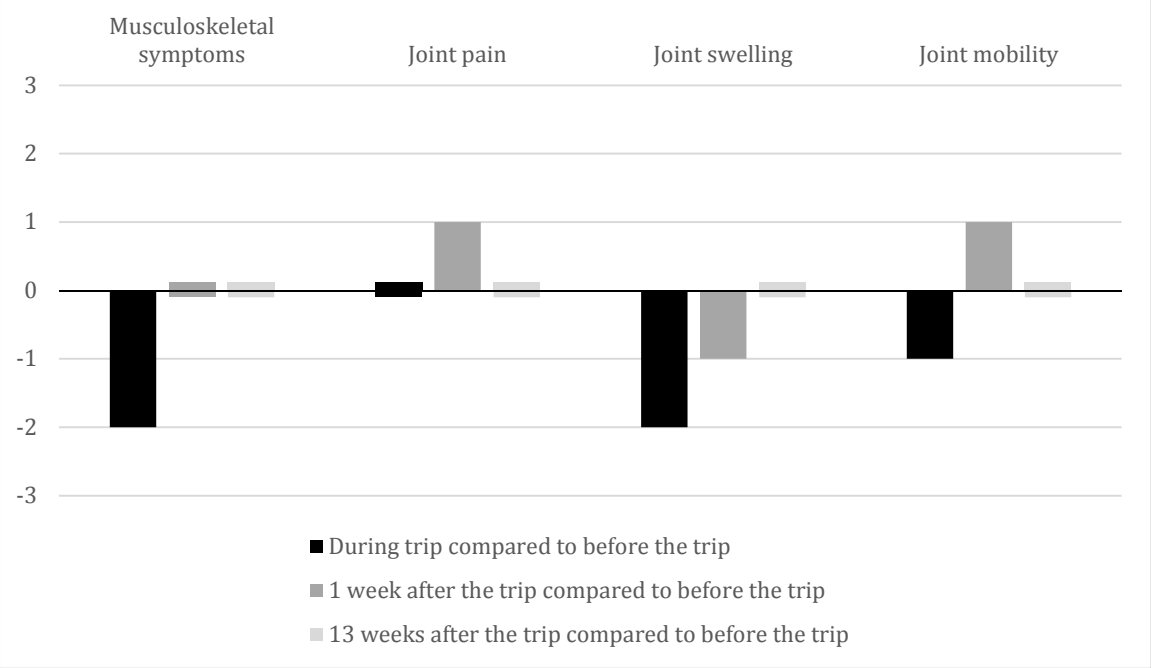

Table 1: Baseline and travel characteristics

		all (274) n(%) or median (IQR)	rheumatic* (65) n(%)	controls (209) n(%)	p-value
Female		157 (57.3)	44 (67.7)	113 (54.1)	0.052
Age (years)		48.5 (32.1-59.5)	48.5 (34.6-57.3)	48.9 (31.7-61.0)	0.89
Nationality (Swiss)		215 (78.5)	50 (76.9)	165 (79.0)	0.99
Other (non-rheumatic) chronic diseases**		90 (32.9)	33 (50.8)	57 (27.3)	<0.001
Destination ****	North America / Europe	57 (13.2)	44 (41.5)	13 (4.0)	<0.001
	Destinations outside Europe/North America	374 (86.8)	62 (58.5)	312 (96.0)	
	Top Five	South Africa 30 (7.0)	Italy 8 (7.6)	South Africa 28 (8.6)	
		India 20 (4.6)	Portugal 7 (6.6)	India 18 (5.5)	
		Thailand 20 (4.6)	Spain 6 (5.7)	Botswana 16 (4.9)	
		Botswana 17 (3.9)	Thailand 5 (4.7)	Namibia 15 (4.6)	
		Namibia 15 (3.5)	Vietnam 4 (3.8)	Thailand 15 (4.6)	
	Top Five outside Europe/North America	South Africa 30 (7.0)	Thailand 5 (4.7)		
		India 20 (4.6)	Vietnam 4 (3.8)		
		Thailand 20 (4.6)	Cambodia Cuba 3 (2.8)		
		Botswana 17 (3.9)	Colombia		

			India Indonesia Kenya Malaysia Morocco Singapore South Africa United Arab Emirates (each 2 (1.9))		
		Namibia 15 (3.5)			

			Argentina Bolivia Botswana Brazil Brunei Darussalam Burma/Myanmar Chile China Ecuador Egypt Hong Kong Japan South Korea Laos Martinique Mauritius Peru Philippines Qatar Russia Zambia Tanzania Tunisia (each 1 (0.9))		

Travel reason	Tourism	188 (82.8)	37 (80.4)	151 (83.4)	0.05
	Visiting friends and relatives	16 (7.1)	6 (13.0)	10 (5.5)	
	Business / aid project	13 (5.7)	0	13 (7.2)	
	Other ***	10 (4.4)	3 (6.5)	7 (3.9)	
Travel style	Backpacking/low budget	27 (11.1)	7 (12.3)	20 (10.7)	0.01
	Middle class	109 (44.7)	24 (42.1)	85 (45.5)	
	Luxury	69 (28.3)	13 (22.8)	56 (30.0)	
	Other	39 (16.0)	13 (22.8)	26 (13.9)	
Trip Duration (days)		18 (14-24)	14 (8-24)	18 (14-24)	0.0074
Accommodation	Hotel	160 (64.8)	31 (53.5)	129 (68.3)	0.039
	Youth hostel/low budget/guest house	41 (16.6)	9 (15.5)	32 (16.9)	0.80
	Apartment	18 (7.3)	12 (20.7)	6 (3.2)	<0.001
	Local friends/family	25 (10.1)	6 (10.3)	19 (10.1)	0.95

	European friends/family	12 (4.9)	3 (5.2)	9 (4.8)	0.90
	Other accommodation	35 (14.2)	7 (12.1)	28 (14.8)	0.60
Medical access	Stayed in areas with time to medical access >24h	12 (4.9)	3 (5.2)	9 (4.8)	0.91
Contact to mammals/warm-blooded animals		85 (34.7)	23 (39.7)	62 (33.2)	0.36
Travel insurance / pharmacy	Travel health insurance	111 (50.9)	28 (53.9)	83 (50.0)	0.63
	Skin repellent	197 (82.8)	27 (49.1)	170 (92.9)	<0.001
	Insecticide (clothes)	115 (50.9)	16 (30.2)	99 (57.2)	0.001
	Sun screen	210 (89.4)	37 (74.0)	173 (93.5)	<0.001
Travel plan change due to health problems					
Cancelled day programme		15 (6.2)	7 (12.5)	8 (4.3)	0.024
Spent less time on daily programme		24 (9.8)	14 (24.6)	10 (5.3)	<0.001
Strenuous to follow daily programme		17 (7.0)	12 (21.4)	5 (2.7)	<0.001
Shortened trip due to health problems		2 (0.8)	1 (1.8)	1 (0.5)	0.37

[*] rheumatoid arthritis n=28, spondyloarthritis n=19, vasculitis n=8, peripheral psoariasis n=10, (immunosuppressed n=56)

[**]chronic diseases included cancer (breast, cervix, prostate, other), diabetes, chronic hepatitis, lung diseases, kidney diseases, cardiovascular diseases, neurological diseases, psychological diseases and other diseases

[***] other reasons included religious trips (e.g. pilgrimage), internships, studying abroad

[****] numbers may not add up as participants travelled to several destinations

Table 2: Risk factors, risk behaviour and precautions in patients with rheumatic diseases and controls with subtropical/tropical destinations

		all (220) n(%)	rheumatic (33) n(%)	controls (187) n(%)	p-value
Drinks during trip	Can/Bottle	165 (75.0)	27 (81.8)	138 (73.8)	0.32
	Water	195 (88.6)	29 (87.9)	166 (88.8)	0.88
	Tap water	44 (20.0)	4 (12.1)	40 (21.4)	0.22
	Milk (unknown if pasteurized)	66 (30.0)	10 (30.3)	56 (30.0)	0.97
	Fruit juice with ice	92 (41.8)	15 (45.5)	77 (41.2)	0.65
	Beer	142 (64.6)	16 (48.5)	126 (67.4)	0.04
	Wine	144 (65.5)	19 (57.6)	125 (66.8)	0.30
	Long drink with ice	113 (51.4)	20 (60.6)	93 (49.7)	0.35
	Long drink without ice	33 (15.0)	4 (12.1)	29 (15.5)	0.62
Food / hygiene during trip	Food stand	61 (27.7)	9 (27.3)	52 (27.8)	0.95
	Raw fish	45 (20.5)	6 (18.2)	39 (20.9)	0.73
	Seafood	73 (33.2)	11 (33.3)	62 (33.2)	0.98
	Raw meat	11 (5.0)	4 (12.1)	7 (3.7)	0.04
	Fruits with skin	89 (40.5)	13 (39.4)	76 (40.6)	0.89
	Fruits not peeled by oneself	122 (55.5)	14 (42.4)	108 (57.8)	0.10
	Salad self-prepared	31 (14.1)	9 (27.3)	22 (11.8)	0.02
	Salad not self-prepared	150 (68.2)	20 (60.6)	130 (69.5)	0.31
	Raw vegetables	121 (55.0)	21 (63.6)	100 (53.5)	0.28
	Hot food on the plane	194 (88.2)	29 (87.9)	165 (88.2)	0.95
	Raw food on the plane	127 (57.7)	22 (66.7)	105 (56.2)	0.26
	Washing / disinfecting hands regularly before eating	145 (66.5)	24 (72.7)	121 (65.4)	0.56
Mosquito protection	Mosquito protection day / evening	186 (84.6)	25 (75.8)	161 (86.1)	0.13
	Mosquito protection night / sleeping	166 (75.5)	23 (69.7)	143 (76.5)	0.41